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SUMMARY WITH CRITICAL APPRAISAL

Acceptance and Commitment Therapy for Post-Traumatic Stress Disorder, Anxiety, and Depression: A Review of Clinical Effectiveness

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Context and Policy Issues

Mental health disorders commonly affect military personal and can lead to functional impairment, disability, inability to perform military duties and even release from service.[1] Based on a systematic review of the literature, the estimated prevalence of combat-related post-traumatic stress disorder (PTSD) in military personnel and veterans is variable, occurring in 2% to 17% of those deployed.[2] Post-traumatic stress disorder (PTSD) occurs following a traumatic event involving death or serious injury or threat of death or serious injury.[3] The individual persistently re-experiences the event through intrusion symptoms (such as recurrent, involuntary, and intrusive memories, traumatic nightmares), and may develop other symptoms such as avoidance behaviours (such as efforts to avoid activities, places, or people that arouse recollections of the trauma), negative alterations in cognitions and mood (such as inability to recall key features of the traumatic event), alterations in arousal (such as difficulty falling or staying asleep) and reactivity (such as exaggerated startle response).[3] The symptoms of PTSD can cause significant distress and functional impairment.

Other psychiatric conditions are also prevalent in military populations, with anxiety disorders and depression commonly affecting those who have served in conflict areas (e.g., Iraq).[4] Canadian data suggest that a service-related mental disorder occurred in approximately 13.5% of personnel who were deployed for the mission in Afghanistan within 4 years of returning.[2]

Cognitive and behavioral therapies (i.e., cognitive behavioural therapy or CBT) have been used to treat PTSD[5] and other psychiatric conditions such as depression[6] and anxiety.[7] Acceptance and Commitment Therapy (ACT) is a more recently introduced form of psychotherapy that focusses on mindfulness and acceptance. [8] According to ACT's underlying theory, mental health disorders result from attempting to avoid a past experience; thus, a goal of treatment with ACT is to develop more accepting, mindful attitudes towards distressing memories and negative conditions rather than avoiding them.[8,9] Other psychotherapies, such as CBT, are more focused on symptom reduction and change.[9] ACT largely involves exercises, role-playing, and metaphors as part of treatment[9] to address six core processes: acceptance, defusion, present moment awareness, self-as-context, values, and committed action.[10] Acceptance and commitment therapy can be delivered one-to-one or in group settings, with the number of sessions required individualized to meet the patient's needs.[8]

The purpose of this report is to summarize the evidence of clinical effectiveness of ACT in adult patients with trauma-related post-traumatic stress disorder, anxiety, or depression, in particular in military veterans.

Research Question

What is the clinical effectiveness of acceptance and commitment therapy for adult patients with trauma-related post-traumatic stress disorder, anxiety, or depression?

Key Findings

Two systematic reviews, two randomized controlled trials and four non-randomized studies (NRSs) assessed the clinical effectiveness of ACT for adult patients with trauma-related PTSD, anxiety, or depression. The two systematic reviews included a limited number of case reports and poor quality studies, but found preliminary evidence supporting the use of ACT in PTSD. One of the two RCTs found favourable results for ACT combined with treatment as usual (TAU) compared to TAU alone in survivors of interpersonal trauma. In comparison to Person-Centred Therapy, ACT had similar outcomes on depression, anxiety, disability, PTSD symptoms, anger, and HRQoL in military veterans. In the four NRSs, ACT had a favourable impact on depression, HRQoL, PTSD symptoms and psychological well-being. However, these studies have a number of methodological limitations that should be considered in their interpretation.

Methods

Literature Search Methods

A limited literature search was conducted on key resources including PubMed, PsycInfo, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was limited to English language documents published between January 1, 2012 and August 1, 2017.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adults with trauma-related post-traumatic stress disorder, anxiety, depression, or a combination of these conditions
Intervention	Acceptance and commitment therapy
Comparator	Alternative psychological treatments (e.g., cognitive behavioural therapy, cognitive processing therapy, prolonged exposure, deep brain processing, eye movement desensitization and reprocessing); Treatment as usual; No treatment or wait-list
Outcomes	Symptoms, as measured by validated scales (e.g., Beck Depression Inventory, Clinician-Administered PTSD Scale, Hamilton Anxiety Scale); Health-related quality of life
Study Designs	Health technology assessments (HTA), systematic reviews (SR), meta-analyses (MA), randomized controlled trials (RCTs), non-randomized studies

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, were individual studies published in a selected systematic review (SR), or were published prior to 2012.

Critical Appraisal of Individual Studies

The included systematic reviews were critically appraised using the AMSTAR checklist,[11] randomized controlled trials were critically appraised using the appropriate SIGN 50 checklists,[12] and non-randomized studies were critically appraised using the Downs and Black checklist.[13] Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations of each included study were described.

Summary of Evidence

Quantity of Research Available

A total of 596 citations were identified in the literature search. Following screening of titles and abstracts, 552 citations were excluded and 44 potentially relevant reports from the electronic search were retrieved for full-text review. One potentially relevant publication was retrieved from the grey literature search. Of these potentially relevant articles, 37 publications were excluded for various reasons, while 8 publications met the inclusion criteria and were included in this report. Appendix 1 describes the PRISMA flowchart of the study selection.

Summary of Study Characteristics

Details of the individual study characteristics are provided in Appendix 2.

Systematic Reviews

Two systematic reviews[14,15] reported on the clinical effectiveness of ACT in a subgroup with a trauma-related anxiety disorder and therefore met the inclusion criteria for this Rapid Response. The characteristics of these systematic reviews are summarized in Appendix 2, Table A2.

Study Design

Systematic reviews did not restrict on the study designs that they included.[14,15] While a larger number of studies were included in both systematic reviews, three studies were included in each. One systematic review published in 2014 included three case study reports of ACT to treat adult patients with PTSD.[15] Another systematic review published in 2013 included two “between-groups studies” in veterans (one study with a non-equivalent control group design and one study in which two groups that received different ACT interventions were compared) and one case study in an adult with PTSD.[14]

Country of Origin

One systematic review was performed by a US-based group[15], while the other was performed by an Australian-based group.[14]

Patient Population

Both systematic reviews[14,15] included populations with anxiety related to a number of different causes, for example, PTSD, general anxiety disorder (GAD), obsessive compulsive disorder (OCD), social anxiety disorder (SAD), but for one systematic review, it was required that the patients had to have a diagnosed anxiety disorder according to the Diagnostic Statistical Manual of Mental Disorders (DSM).[14]

Interventions and Comparators

While both systematic reviews assessed the effectiveness of ACT, the intervention was defined differently in the two systematic reviews, resulting in different literature being included. In one systematic review, in order to be included, the effects of ACT had to be quantified using the Acceptance and Action Questionnaire, which is a measure of psychological flexibility or inflexibility.[15] In the other systematic review, studies were included that employed a minimum of two core ACT processes.[14] No comparator was required in either systematic review.[14,15]

Outcomes

In one systematic review, only anxiety symptoms were included as outcome measures,[15] whereas the other systematic review considered any outcome that was measured with an instrument or questionnaire that had established psychometric properties.[14] There was no specific duration of follow-up required post-treatment in either systematic review for study inclusion.[14,15]

Clinical Studies

Six clinical studies[4,16-20] met the inclusion criteria for this Rapid Response, the characteristics of which are summarized in Appendix 2, Table A3.

Study Design

Two parallel group randomized controlled trials (RCTs)[4,16] and four non-randomized studies (NRS)[17-20] were included. The NRSs were all single group studies that involved a pre-treatment (baseline) assessment, followed by the intervention, then a post-treatment assessment. [17-20] The RCTs differed in their duration of follow-up, with one RCT re-assessing patients immediately post-treatment (i.e., at 10-weeks), with no further follow-up[16], while the other RCT included an immediate post-treatment assessment as well as multiple follow-up assessment up to 12 months.[4] The duration of follow-up of the NRSs ranged from four weeks[18] to 16 weeks weeks[19], with no outcome assessment beyond the immediate post-treatment assessment in any study.[17-20]

Country of Origin

All six clinical studies were carried out in the United States.[4,16-20]

Patient Population

One RCT included a population of veterans of Operations Enduring Freedom, Iraqi Freedom, or New Dawn who had any anxiety or depressive disorder or post-concussive symptoms.[4] The other RCT included traumatized participants from a community outreach program with symptoms of PTSD.[16] Three of the NRSs included populations of veterans,[18-20] while the other included women with a history of interpersonal trauma who were recruited

from local mental health and community agencies.[17] One NRS included veterans with a number of different disorders, including unspecified depressive and anxiety disorders, major depressive disorder, adjustment disorders, and PTSD[18], while the other two included veterans with a diagnosis of depression who were not in acute crisis.[19,20] The veteran populations were predominately male,[4,18-20] while the community outreach program participants were predominantly or exclusively female.[16,17]

Interventions and Comparators

The ACT intervention in the two RCTs differed in duration. In one RCT, the participants received four one-hour sessions of ACT, in addition to treatment as usual (TAU), which was defined as various cognitive behavioural therapies.[16] The control group received TAU as the comparator. In the other RCT, the ACT intervention was delivered as 12, 60-minute sessions that occurred on a weekly basis.[4] A previously developed manual was used to guide the delivery of the intervention.[4] The comparator group received a psychotherapy, person-centred therapy or PCT, which was also delivered as 12, 60-minute sessions that occurred on a weekly basis.[4]

The NRS in women with interpersonal trauma delivered the ACT intervention as a six separate web-based sessions that were approximately one hour long each.[17] One NRS in veterans used a focussed ACT intervention, referred to as focused acceptance and commitment therapy (FACT), which was four weeks long and consisted of 90 minute sessions. The remaining two NRS uses the same ACT protocol that was developed for the treatment of depression for use in the United States Department of Veterans Affairs.[17,19] It involves a standardized 12 to 16 week psychotherapy protocol that is delivered by trained therapists.[17,19]

Outcomes

A number of scales were used to measure outcomes of ACT in the included RCTs and NRSs. Symptoms of PTSD were measured with different versions of PTSD Checklist (PCL), which included the PCL-S (the "Specific" Version"),[16] the PCL-M (the "Military Version,[4] and the PCL-5 (which measures symptoms according to the DSM-5).[17] The Beck Depression Index-II (BDI) was used in three studies to measure symptoms of depression.[16,19,20] The Depression Anxiety and Stress Scale 21 (DASS-21) was used in two studies.[17,18] Health related quality of life (HRQoL) was assessed in three studies using the WHOQOL-BREF[4,20] and the SF-12.[4,18] Other outcomes and outcome measures that were assessed a single study included depression, anxiety and somatization measured with the Brief Symptom Inventory-18 Global Severity Index (BSI-18 GSI)[4], the Sheehan Disability Scale (SDS),[4] the Dimensions of Anger Reactions-II,[4] depression measured with the Patient Health Questionnaire 9 (PHQ-9),[4] and the WBI-5 Well-being Index which assesses psychological well-being.[18]

Summary of Critical Appraisal

Additional details regarding the strengths and limitations of included publications are provided in Appendix 3 Table A4 (Systematic Reviews), Table A5 (Randomized Controlled Trials) and Table A6 (Non-randomized Studies).

Systematic Reviews

The systematic review performed by Bluett et al.[15] had a number of limitations. The selection criteria for inclusion of studies into the systematic review were not clearly

presented in the publication. While it was stated that the effects of ACT had to be quantified with the Acceptance and Action Questionnaire for studies to be included, additional inclusion or exclusion criteria were not reported. Further, the methods for study selection and data extraction were not reported. The literature search focused on two psychology databases and it did not appear that a grey literature search was performed. Limited characteristics of the included studies were provided and limited details of the individual study populations were presented. No quality assessment of the included studies was performed. Strengths of this systematic review would include a clearly stated research question and appropriate statistical analysis and use of narrative summary where applicable. Publication bias was assessed using multiple methods.

The systematic review performed by Swain et al.[14] reported the methodology used in greater detail. The literature search appeared to be comprehensive and included a grey literature search. Screening and study selection occurred in duplicate and data extraction was performed with a standardized data extraction sheet. Quality assessment was performed with a checklist for psychotherapy studies and was performed by two reviewers, with the results of the quality assessment being considered in the discussion of the paper. The analysis methods appeared to be appropriate with a narrative synthesis being chosen due to heterogeneity between studies. Limitations of the review included a lack of assessment of publication bias and no statement of conflict of interest.

Randomized Controlled Trials

While the study addressed a clearly defined research question and used standard, valid and reliable instruments to measure outcomes, Boals et al.(2016)[16] had a number of important limitations. Importantly, randomization in the study was not maintained as several patients who were randomized to the control group (TAU) received ACT instead when other patients failed to show up. This resulted in an imbalance in the size of the study groups with the ACT group having 37 of the 63 patients enrolled compared with 26 patients in the TAU group. Further, methods for randomization and allocation concealment were not described. Baseline characteristics were not described according to each group and the authors noted that there were some differences at baseline. Importantly, there were differences at baseline in scores on the Beck Depression Index-II (BDI-II) and the PTSD Symptom Checklist (PCL-S). This creates challenges in interpreting the statistical analyses and in making comparisons between groups for the change from baseline. Further, no information was provided on the use of co-interventions, such as pharmacotherapies, therefore it is unclear if the two groups were treated equally aside from the intervention. The number of drop-outs was high in both treatment arms, with approximately one-third of patients failing to complete treatment. An intention to treat analysis of the data was not performed.

Lang et al.,(2016) had similar limitations to Boals et al.(2016)[16] but had some additional strengths. Lang et al.(2016) was a multi-site study. While results were not reported by site, efforts were made (through training) to standardize treatment across sites. Failure to complete treatment was high, with 53% of participants completing 12 sessions of ACT and 64% of participants completing 12 sessions of PCT. However, the loss to follow-up was less than 10% in each arm and an intention to treat analysis of the data was performed. Background use of psychotropic medications was quantified, with use appearing to be higher in the PCT group. No data were provided on the type of medications used. Strengths of Lang et al.(2016) included appropriate methods of randomization and allocation

concealment, a detailed presentation of baseline characteristics and use of standard, valid and reliable instruments to measure outcomes.

Non-randomized Studies

The key limitation of the included NRSs is a lack of a control group to which to compare the effects of ACT. Without a control for comparison, it is difficult to attribute any changes from baseline or pre-treatment that observed solely to the intervention that the ACT group received. However, the quality of the included NRSs was assessed with items from the Downs and Black Checklist[13] that are applicable to single group studies and are summarized in Appendix 3 Table A6.

The NRSs asked clear and focused research questions, adequately described the outcomes to be measured, included patients, interventions of interest, main study findings, had accurate and reliable outcome measures, and appropriately reported the statistical results.[17-20] Only one study had an a priori power calculation.[17] It appeared that the staff and facilities where the patients were treated were reflective of the treatment the majority of patients would receive.[17-20] For example, two studies delivered ACT according to the protocol designed for and used by United States Veterans Health Administration.[19,20] Limitations common to the NRSs included a lack of description of the screening population.[17-20] It was unclear in the four NRSs how many individuals had been asked to participate but refused and how those individuals differed from participants. Thus, it was unclear if the participants were representative of the larger population. There was significant loss to follow-up, attrition or failure to complete the ACT sessions in three of the NRSs, ranging from 16% to 34%.[17,19,20] There were no descriptions of how completers differed from non-completers in any of the studies.[17,19,20] Two studies did not account for potential confounders in their statistical models.[17,18]

Summary of Findings

Additional details regarding the main study findings and authors' conclusions are provided in Appendix 4 Table A7 (Systematic Reviews) and Table A8 (Clinical Studies).

Systematic Reviews

Bluett et al.(2106)[15] briefly summarized three case studies in which ACT was used to treat PTSD in adults, one involving a veteran, one involving an adult with PTSD and substance abuse and one involving an adult with depression and PTSD. No details were provided. It was only stated that all cases provided preliminary support for ACT. The authors made no conclusions specific to PTSD, but noted that the evidence supporting the use of ACT in anxiety disorders was promising, but required further research.

Swain et al.(2016)[14] briefly summarized two comparative studies and one case report of ACT for the treatment of PTSD. One study compared two different versions of ACT in a total of 15 veterans and found both groups improved with respect to PTSD scores, symptoms and distress. A second study compared ACT in 12 veterans to demographically matched controls without PTSD who received no intervention. They found that patients with ACT experienced an increase in automatic thoughts relative to controls. The third study that was included was a case study in which a woman received 21 individual ACT sessions to manage chronic PTSD and major depressive disorder, she experienced an improvement in PTSD severity and anxiety. The authors noted difficulties in drawing conclusions about the effectiveness of ACT in the treatment of PTSD due to the limited evidence and quality of the evidence available.

Randomized Controlled Trials

Boals et al.(2016)[16] found that immediately after treatment, the decrease in PCL-S scores with ACT plus TAU was greater than TAU alone, but at six weeks post-treatment there was no difference in between groups in the amount of change from baseline. For BDI-II scores, the change from pre-treatment was greater with ACT plus treatment immediately post-treatment and at six weeks post-treatment. The authors concluded that the addition of ACT to TAU resulted in significant decreases in in symptoms of PTSD and depression.

Lang et al.(2016)[4] found that there were no statistical differences between ACT and PCT immediately post-treatment, three months after treatment and 12 months after treatment for the BSI-18 GSI and the SDS, which were the primary outcomes of the study. For the secondary outcomes, which were only assessed immediately post-treatment, there were no statistical differences in the improvement from baseline in the PHQ-9, PCL-M, DAR-II, and the four domains of the WHOQOL-BREF. The authors concluded that both ACT and PCT were associated with modest treatment effects and that ACT performed similarly to PCT. They did not endorse ACT as a first-line treatment approach amongst veterans.

Non-randomized Studies

Fiorillo et al.(2017)[17] assessed web-based ACT in individuals who had experienced interpersonal trauma and found statistically significant improvements from baseline in the PCL-5 and the depression and anxiety scales of the DASS-21 immediately post-treatment. The authors concluded that ACT delivered in this manner may be beneficial in this population and that further study using an RCT design was warranted.

Glover et al.[18] assessed a focused ACT intervention in veterans with a number of different diagnoses and found statistically significant improvements over baseline in the depression and stress scales of the DASS-21, the physical and mental health composite scores of the SF-12, and the WBI-5, but statistically non-significant improvements in the anxiety scale of the DASS-21 immediately post-treatment.

Wasler et al., 2015[19] and Wasler et al, 2013.,[20] assessed ACT in veterans with depression found statistically significant improvements in scores on the BDI-II in both studies,[19,20] a reduction in the proportion of patients reporting suicidal ideation,[19] and improvements in all domains of the WHOQOL-BREF[20] immediately post-treatment. Based on these findings, the authors concluded that there was evidence to support ACT for the treatment of depression.[19,20]

Limitations

The included systematic reviews captured a limited amount of literature specific to the clinical effectiveness of ACT in trauma-related mental health disorders such as PTSD, depression and anxiety.[14,15] They generally included case studies or comparative studies that were considered poor quality. As such, despite being systematic reviews, they provided limited additional evidence beyond the clinical studies that met the inclusion criteria for this report.

In addition to the limitations noted in the critical appraisal section of this report, other potential methodological issues may be considered when interpreting the findings of the RCTs and NRSs. Failure to complete the ACT sessions according to the study protocol occurred frequently in some of the studies.[4,16,19,20] This could potentially compromise the effectiveness of the ACT interventions received by participants. Lack of adherence to the

intervention may also bring into question how successful these interventions would be in real-world settings if patients are unwilling to participate fully. The ACT interventions differed across studies, with the exception of two NRSs which used the same standardized training protocol.[19,20] This makes it difficult to make comparisons across studies and could be one factor that contributed to differences in outcomes. The training received by the individuals delivering the intervention was not described in one study.[16] Thus, it was not clear if ACT was delivered in a standardized manner within this study.

Only one study[4] reported on concurrent use of psychotropic medication, but provided limited information. Concurrent psychotropic medication use is an important co-intervention. It is unclear what effect concomitant medication use could potentially have had on the observed results. Only one study reported on outcomes beyond the time point immediately post-treatment[4] and did so for a limited number of outcomes in that study. It is unclear if the observed treatment effects would be maintained longer-term without sustained or ongoing intervention. As the NRSs lacked control groups, it is not possible to establish a causal relationship between the observed outcomes and ACT. This is particularly important since the outcome measures were subjective assessments and the patients were aware of their treatment status. Further, the studies generally involved individuals who were seeking treatment; thus, they may have had the desire to improve. These factors emphasize the importance of having a control group for comparison.

All studies were performed in United States-based settings. It is not clear if they are generalizable to the Canadian context. Further, some studies were performed in groups that had experienced interpersonal trauma.[16,17] The generalizability of the findings of these studies to groups that have experienced other types of trauma may be limited.

Conclusions and Implications for Decision or Policy Making

Two systematic reviews, two RCTs and four NRSs assessed the clinical effectiveness of ACT for adult patients with trauma-related PTSD, anxiety, or depression. The two systematic reviews offered limited evidence informing the research question for this report. Based upon the clinical studies, the clinical effectiveness of ACT was somewhat conflicting depending on the population and study design. In survivors of interpersonal trauma, ACT reduced symptoms of PTSD and depression. While these findings are based on an RCT design, the generalizability of this study to other populations maybe limited. Modest treatment effects were observed with ACT in an RCT carried out in veterans, with no statistical differences being found between ACT and a control psychotherapy condition on a number of patient reported outcomes (symptoms, quality of life, disability). Non-randomized studies using single group, pre-treatment/post-treatment designs have found favourable results with ACT, but without a control for comparison it is difficult to attribute the observed improvement in outcomes directly to the intervention. With these limitations noted, two NRSs in veterans found improvements in depressive symptoms and HRQoL immediately post-treatment with ACT, and one study in veterans affected by different mental health disorders found improvements in depression, stress and HRQoL. Longer-term follow-up data were unavailable. Further evaluation of ACT in randomized controlled trials with assessment of outcomes over a longer time period post-intervention is warranted.

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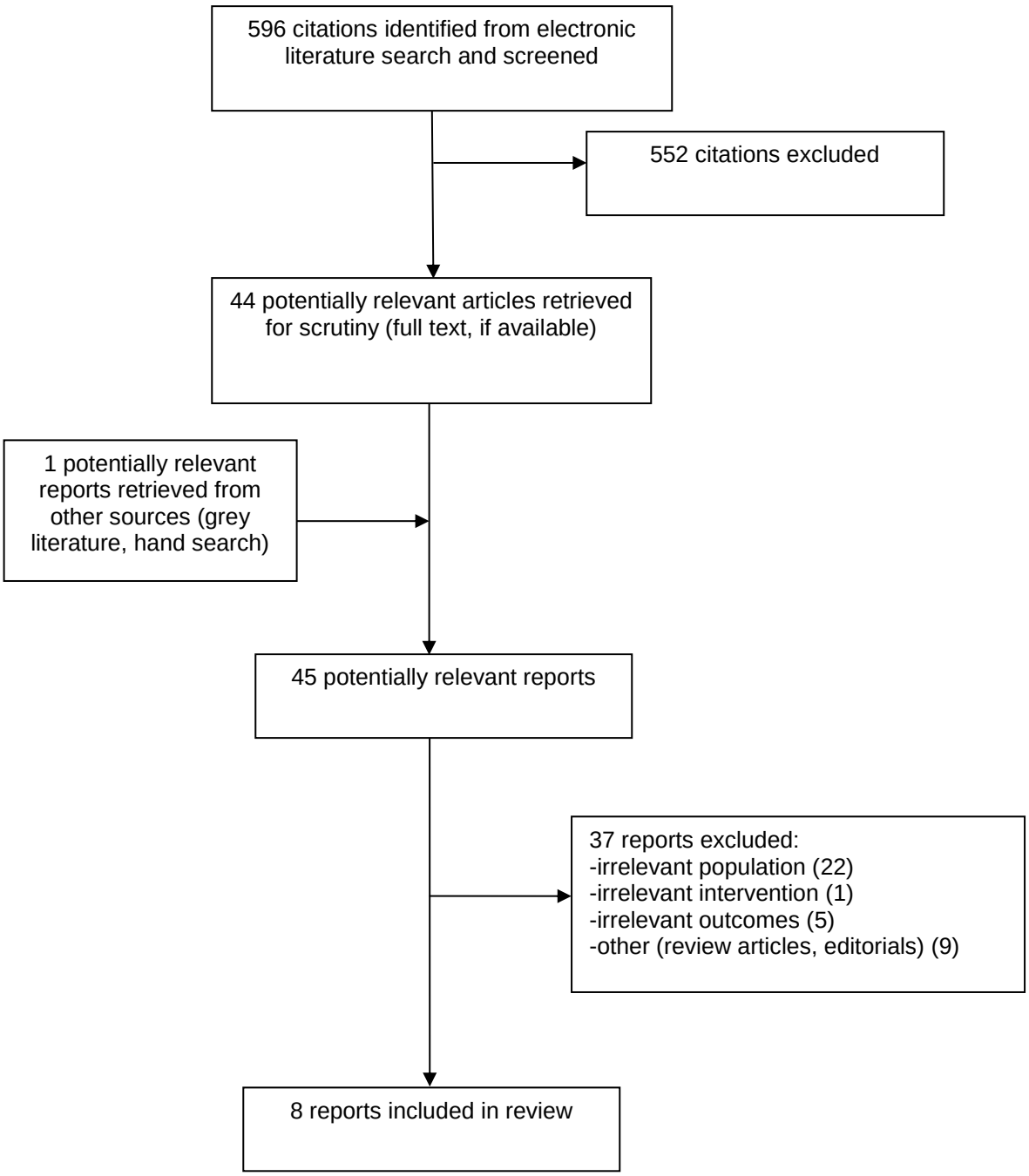
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table A2: Characteristics of Included Systematic Reviews

First Author, Publication Year, Country	Types and Numbers of Primary Studies Included	Population Characteristics	Intervention	Comparator	Clinical Outcomes, Length of Follow-up
Bluett et al. 2014[15] United States	49 articles were included in total, 3 of which were in patients with PTSD and were case studies. There was no restriction on study design. Additional studies were included in the SR that involved populations that had experienced traumatic events, but outcome data were pooled with other non-trauma populations.	Patients with anxiety symptoms related to a number of different psychiatric disorders (e.g., GAD, OCD, PTSD, SAD). The PTSD group was considered relevant to this Rapid Response.	ACT – the effects of which had to be quantified with the Acceptance and Action Questionnaire (a measure of psychological flexibility/ inflexibility)	No comparator required	Anxiety symptoms with no specific length of follow-up required.
Swain et al. 2013[14] Australia	39 articles were included in total (there was no restriction on study design), 3 of which were in patients with PTSD (two studies which were described as between group studies in veterans and one case study). The remaining studies stated the type of anxiety disorder, not the underlying cause, and did not identify veteran populations. Thus, trauma-related anxiety or populations of veterans could not be identified from these studies.	Patients with an anxiety disorder as defined by the Diagnostic Statistical Manual of Mental Disorders. The PTSD group was considered relevant to this Rapid Response.	ACT employing a minimum of two core processes.	No comparator required	Outcome measures of established psychometric properties.

ACT = Acceptance and commitment therapy; GAD = Generalized anxiety disorder; OCD = Obsessive compulsive disorder; PTSD = Post-traumatic stress disorder; SR= Systematic review

Table A3: Characteristics of Included Clinical Studies

First Author, Publication Year, Country	Study Design, Length of Follow-up	Patient Characteristics, Sample Size (n)	Intervention	Comparator(s)	Clinical Outcomes
Randomized Controlled Trials					
Boals et al., 2016[16] United States	Parallel group, RCT 10 week follow-up period (post-treatment assessment immediately following the final ACT session and 6 weeks later)	Traumatized participants from a community outreach centre who reported elevated symptoms of PTSD. Participants did not have to meet DSM-IV criterion of their most stressful event being life threatening (many life events were abuse, family and domestic violence). Average age: 35.7 (range 22 – 52) Female: 97% Caucasian: 76% n=63 completed pretreatment assessment n=42 completed 6-week post-treatment assessment	TAU plus 4 1-hour sessions of ACT. The sessions heavily emphasized the self-as-context component of ACT. "*The ACT intervention targeted experiential avoidance using didactics, experiential exercises, and metaphor. During all four ACT sessions, the therapists employed a special emphasis on contact with the present moment and on skills related to the decentralizing of trauma and broadening of the self-concept.*" (p.476)	Control condition of TAU – "*variations of cognitive behavioural therapies in the context of a person-centred approach.*" (p. 476)	PCL-S (PTSD Checklist – Measures symptoms of PTSD) BDI-II (Measures symptoms of depression)
Lang et al., 2016[4] United States	Parallel group RCT 12 months of follow-up at multiple time points.	Veterans of Operations Enduring Freedom, Iraqi Freedom, or New Dawn who had any anxiety or depressive disorder or post-concussive symptoms. Average age: 34.2	ACT – Delivered according to a previously developed manual with 12 weekly, 60-minute sessions. *"The key focus of the manual was on addressing experiential*	Present-centred therapy – *"a manualized psychotherapy that focuses on current life concerns, the connection between those concerns and the individual's*	**Primary** Brief Symptom Inventory-18 Global Severity Index (Measures depression, anxiety and somatization) Sheehan Disability Scale (Measures disability)

Table A3: Characteristics of Included Clinical Studies

First Author, Publication Year, Country	Study Design, Length of Follow-up	Patient Characteristics, Sample Size (n)	Intervention	Comparator(s)	Clinical Outcomes
		(SD = 8) Male: 80% White: 75% n=160 randomized and analyzed.	*avoidance and the problem of excessive control of internal experience more broadly, while also focusing on values-based behavior change."* (p.5)	*symptoms, and client-directed problem solving."* (p.2) PCT was delivered as 12 weekly, 60-minute sessions.	**Secondary** PHQ-9 (Measures depression) PCL-M (PTSD Checklist Military Version– Measures symptoms of PTSD) DAR-II (Measures anger towards others) SF-12 (Measures HRQoL) WHOQOL-BREF (Measures HRQoL)
Non-randomized Studies					
Fiorillo et al., 2017[17] United States	Single group study with a pre-intervention/post-intervention design. 6 week study, with post-treatment evaluation immediately following the last session (no further follow-up occurred).	*"Women over the age of 18 with a history of interpersonal trauma in the form of childhood sexual and/or physical abuse, adolescent or adult sexual assault, or partner violence".* (p105) Recruited from local mental health and community agencies. Average age: 39.1 (SD = 16) Female: 100% White: 76% n = 25 enrolled and analyzed.	ACT – *"The intervention consisted of six separate web-based multimedia sessions, each approximately an hour long, covering the following content areas: introduction and psychoeducation on interpersonal trauma and ACT, willingness and acceptance, mindfulness, defusion and self-as-context, clarifying values, and committed action consistent with values."* (p.106)	No intervention (Patient's own pre-treatment scores).	PCL-5 (PTSD Checklist – Measures symptoms of PTSD according to the DSM-5) DASS-21 (Measures symptoms of depression, anxiety and stress)

Table A3: Characteristics of Included Clinical Studies

First Author, Publication Year, Country	Study Design, Length of Follow-up	Patient Characteristics, Sample Size (n)	Intervention	Comparator(s)	Clinical Outcomes
Glover et al., 2016[18] United States	Single group study with a pre-intervention/post-intervention design. 4 week study, with post-treatment evaluation immediately following the last session (no further follow-up occurred).	Veterans with unspecified depressive and anxiety disorders, major depressive disorder, adjustment disorders, and PTSD. Average age: 53.2 (SD = 13) Male: 86% Caucasian: 64% n = 51 enrolled and analyzed	FACT – "*The FACT group in this protocol consisted of four 90-min, weekly group sessions: Finding Leverage, Promoting Awareness, Promoting Openness, and Promoting Engagement.*" (p.158)	No intervention (Patient's own pre-treatment scores).	WBI-5 (Measures psychological well-being) DASS-21 (Measures symptoms of depression, anxiety and stress) SF-12 (Measures HRQoL)
Wasler et al., 2015[19] United States	Single group study with a pre-intervention/post-intervention design. Unclear reporting, but appeared to be 10 to 16 weeks, with post-treatment evaluation immediately following the last session (no further follow-up occurred).	Veterans with a diagnosis of depression who were not in acute crisis and were appropriate candidates for psychotherapy. Average age: 50.5 (SD = 12.5) Male: 76% White: 72% n = 981 enrolled with final analysis sample ranging from 520 to 629.	ACT - *"The ACT for Depression treatment protocol was developed specifically for veterans and is intended to be administered in approximately 12 - 16 individual psychotherapy sessions."* (p.26)	No intervention (Patient's own pre-treatment scores)	BDI-II (Measures symptoms of depression) Suicidal Ideation
Wasler et al., 2013[20] United States	Single group study with a pre-intervention/post-intervention design. Unclear reporting, but appeared to be	Veterans with a diagnosis of depression who were not in acute crisis and were appropriate candidates for	ACT - *"The protocol used during the Training Program was based on the structure and format of the 12-session protocol contained in*	No intervention (Patient's own pre-treatment scores)	BDI-II (Measures symptoms of depression) WHOQOL-BREF (Measures HRQoL)

Table A3: Characteristics of Included Clinical Studies

First Author, Publication Year, Country	Study Design, Length of Follow-up	Patient Characteristics, Sample Size (n)	Intervention	Comparator(s)	Clinical Outcomes
	12 weeks, with post-treatment evaluation immediately following the last session (no further follow-up occurred).	psychotherapy. Average age: 51 (SD = 12) Male: 76% White: 73% n = 745 enrolled with final analysis sample of approximately 420	*ACT for Depression: A Clinician's Guide to Using Acceptance & Commitment Therapy in Treating Depression (Zettle, 2007). A 12-session manual specific to the delivery of ACT for depression with Veterans was developed and provided to training participants to complement the Zettle (2007) manual."* (p.556)		

ACT = Acceptance and commitment therapy; BDI-II = Beck Depression Inventory-II; DAR-II = Dimensions of anger reactions; DASS-21 = Depression Anxiety and Stress Scale 21; DSM= Diagnostic and Statistical Manual of Mental Disorders; FACT = Focused acceptance and commitment therapy; HRQoL = Health-related quality of life; PHQ-9: Patient Health Questionnaire 9; PCL-S = PTSD Checklist Specific; PCT = Present–Centered Therapy; PTSD = Post-traumatic stress disorder; RCT = randomized controlled trial; SD = Standard deviation; SF-12 = Short Form 12;TAU = Treatment as usual; WBI-5 = WHO-5 Well Being Index; WHOQOL-BREF = World Health Organization Quality of Life Scale, Brief

Appendix 3: Critical Appraisal of Included Publications

Table A4: Strengths and Limitations of Systematic Reviews and Meta-Analyses using the AMSTAR Checklist[11]

Strengths	Limitations
Bluett et al. 2014[15]	
Was an a priori design provided? • The research questions were clearly defined. **Was the status of publication (i.e. grey literature) used as an inclusion criterion?** • No reports were excluded based on publication type. **Were the methods used to combine the findings of studies appropriate?** • Random effects models were used to combine the studies for other indications. • For PTSD, studies were summarized narratively which appeared to be appropriate. **Was the likelihood of publication bias assessed?** • Publication bias was assessed using funnel plots, trim and fill, and fail safe N.	**Was an a priori design provided?** • The inclusion criteria were not well defined and the PICO dimensions were not clearly stated. **Was there duplicate study selection and data extraction?** • Methods for study selection and data extraction were not reported. **Was a comprehensive literature search performed?** • The literature search included only psychology databases, but did not search other databases or the grey literature. **Was a list of studies (included and excluded) provided?** • A list of excluded studies was not provided. **Were the characteristics of the included studies provided?** • A limited description of the study population was provided, without any demographic information provided. **Was the scientific quality of the included studies assessed and documented?** • No quality assessment of the included studies was performed. **Was the scientific quality of included studies used appropriately in formulating conclusion?** • No quality assessment of the included studies was performed. **Was conflict of interest included?** • There was no statement of conflict of interest.
Swain et al. 2013[14]	
Was an a priori design provided? • The research questions were clearly defined and the inclusion criteria were clearly stated. **Was a comprehensive literature search performed?** • The literature search appeared to be comprehensive including multiple databases. **Was there duplicate study selection and data extraction?** • Screening and study selection were performed in duplicate. • Data extraction was performed with a standardized sheet but it was unclear if it was performed in duplicate. **Was a list of studies (included and excluded) provided?** • A list of excluded studies was provided in an appendix. **Was the status of publication (i.e. grey literature) used as an inclusion criterion?** • There was no restriction on publication status and grey literature was included.	**Was the likelihood of publication bias assessed?** • Publication bias was not assessed **Was conflict of interest included?** • There was no statement of conflict of interest.

Table A4: Strengths and Limitations of Systematic Reviews and Meta-Analyses using the AMSTAR Checklist[11]

Strengths	Limitations
Were the characteristics of the included studies provided? • The characteristics of the studies and their populations were reported. **Was the scientific quality of the included studies assessed and documented?** • Two independent reviewers assessed the quality of the included studies with the Psychotherapy Outcome Study Methodology Rating Form and the results were reported in the review. **Was the scientific quality of included studies used appropriately in formulating conclusion?** • The results of the quality assessment were considered in the discussion and conclusion. **Were the methods used to combine the findings of studies appropriate?** • The methods appeared to be appropriate. The authors stated that they chose to use a narrative synthesis due to heterogeneity in the included studies.	

Table A5: Strengths and Limitations of Randomized Controlled Trials using the SIGN 50 Checklist[12]

Strengths	Limitations
Boals et al., 2016[16]	
The study addresses appropriate and clearly focused question. • The study question was appropriate. **All relevant outcomes are measured in a standard, valid and reliable way.** • Standardized scale measures such as the PCL-S and the BDI-II were used to measure outcomes.	**The assignment of subjects to treatment groups is randomized.** • Some participants who were randomized to TAU ended up receiving ACT when those randomized to ACT failed to show up for treatment (in order to maintain the treatment group size). • The method of randomization was not described. **An adequate concealment method is used.** • The method of allocation concealment was not described. **Subjects and investigators are kept blind about allocation.** • It is unclear if the participants and investigators were blind to the allocation. It is doubtful given that some participants randomized to TAU were switched over to ACT. **The only difference between groups is the treatment under investigation.** • No information on co-interventions such as pharmacotherapies was provided. Thus, it is unclear if there were differences between groups. **The treatment and control groups are similar at the start of the trial.** • While the baseline demographic characteristics were not presented by group, the authors noted as a limitation that there were differences between groups at baseline. • There were differences at baseline in scores on the BDI-II and PCL-S. This creates challenges in interpreting the statistical analyses and in making comparisons between groups for the change from baseline. **What percentage of subjects in each treatment arm dropped out before the study was completed?** • 35% of the TAU arm and 32% of the ACT group dropped out before the study was completed. **All subjects are analyzed in the groups to which they were randomly allocated (intention to treat analysis).** • The analysis was not intention to treat. It was based off of available cases.
Lang et al., 2016[4]	
The study addresses appropriate and clearly focused question. • The study question was appropriate. **The assignment of subjects to treatment groups is randomized.**	**Subjects and investigators are kept blind about allocation.** • Allocation was concealed until the point of which therapy was delivered. **The only difference between groups is the treatment under investigation.**

Table A5: Strengths and Limitations of Randomized Controlled Trials using the SIGN 50 Checklist[12]

Strengths	Limitations
• Randomization performed in blocks according to site and diagnosis, using a web-based randomizer to ensure allocation concealment. **An adequate concealment method is used.** • A web-based method was used to conceal allocation. **The treatment and control groups are similar at the start of the trial.** • Detailed baseline characteristics were reported and appeared to be balanced between groups. **All relevant outcomes are measured in a standard, valid and reliable way**. • Outcomes were measured using common scales with validated measurement properties. **All subjects are analyzed in the groups to which they were randomly allocated (intention to treat analysis).** • An intention to treat analysis was performed, with all 160 participants being included in the analysis.	• Psychotropic medication use was reported and appeared to be higher in the PCT group (83% versus 90%). **What percentage of subjects in each treatment arm dropped out before the study was completed?** • Attrition was a problem, but a statistical method (MMRM) was used to handle missing data. • 53% of participants received all 12 sessions of ACT • 64% of participants received all 12 sessions of PCT • Loss to follow-up, however, was less than 10% in each arm. **Where the study is carried out at more than one site, results are comparable for all sites.** • It was unclear of the results were the same for all five sites that participated in the trial. Efforts were made to standardize the intervention across sites.

ACT = Acceptance and commitment therapy; BDI-II = Beck Depression Inventory-II;MMRM = Mixed model for repeated measures; PCL-S = PTSD Checklist Specific; PCT = Present–Centered Therapy; PTSD = Post-traumatic stress disorder; TAU = Treatment as usual

Table A6: Strengths and Limitations of Non-Randomized Studies using the Downs and Black Checklist[11]

Strengths	Limitations
Fiorillo et al., 2017[17]	

• **Is the hypothesis/aim/objective of the study clearly described?**
  ○ Yes
• **Are the main outcomes to be measured clearly described in the Introduction or Methods section?**
  ○ Yes
• **Are the characteristics of the patients included in the study clearly described?**
  ○ Some characteristics were described
• **Are the interventions of interest clearly described?**
  ○ Yes
• **Are the main findings of the study clearly described?**
  ○ Yes
• **Does the study provide estimates of the random variability in the data for the main outcomes?**
  ○ Yes
• **Have all important adverse events that may be a consequence of the intervention been reported?**
  ○ Yes
• **Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?**
  ○ Yes
• **Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?**
  ○ Yes – local mental health and community agencies
• **Were the statistical tests used to assess the main outcomes appropriate?**
  ○ Yes
• **Were the main outcome measures used accurate (valid and reliable)?**
  ○ Yes
• **Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance <5%**
  ○ A priori power calculation suggested that the study was adequately powered even with loss to follow-up.
	• **Have the characteristics of patients lost to follow-up been described?**
	  ○ Four patients (16%) dropped out, the characteristics of whom were not described.
	• **Were those subjects who were prepared to participate representative of the entire population from which they were recruited?**
	  ○ Unclear; no information provided on the broader population. Patients were seeking treatment so could be a select, motivated population.
	• **Were the subjects asked to participate in the study representative of the entire population from which they were recruited?**
	  ○ Unclear; no information provided on the broader population. Patients were seeking treatment so could be a select, motivated population.
	• **Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?**
	  ○ No

Glover et al.,(2016)[18]	

• **Is the hypothesis/aim/objective of the study clearly described?**
  ○ Yes
• **Are the main outcomes to be measured clearly**
	• **Have all important adverse events that may be a consequence of the intervention been reported?**
	  ○ No adverse event reporting
	• **Were those subjects who were prepared to**

Table A6: Strengths and Limitations of Non-Randomized Studies using the Downs and Black Checklist[11]

Strengths	Limitations
described in the Introduction or Methods section? ○ Yes • **Are the characteristics of the patients included in the study clearly described?** ○ Some characteristics were described • **Are the interventions of interest clearly described?** ○ Yes • **Are the main findings of the study clearly described?** ○ Yes • **Does the study provide estimates of the random variability in the data for the main outcomes?** ○ Yes • **Have the characteristics of patients lost to follow-up been described?** ○ No loss to follow-up • **Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?** ○ Yes • **Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?** ○ Yes • **Were the statistical tests used to assess the main outcomes appropriate?** ○ Yes • **Were the main outcome measures used accurate (valid and reliable)?** ○ Yes • **Were losses of patients to follow-up taken into account?** ○ No loss to follow-up	**participate representative of the entire population from which they were recruited?** ○ Unclear; patients were referred specifically for the intervention • **Were the subjects asked to participate in the study representative of the entire population from which they were recruited?** ○ Unclear • **Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?** ○ No • **Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance <5%** ○ Unclear
Wasler et al., 2015[19]	
• **Is the hypothesis/aim/objective of the study clearly described?** ○ Yes • **Are the main outcomes to be measured clearly described in the Introduction or Methods section?** ○ Yes • **Are the characteristics of the patients included in the study clearly described?** ○ Some characteristics were described • **Are the interventions of interest clearly described?** ○ Yes • **Are the main findings of the study clearly described?**	• **Have all important adverse events that may be a consequence of the intervention been reported?** ○ No adverse event reporting • **Were those subjects who were prepared to participate representative of the entire population from which they were recruited?** ○ Unclear; the authors did not report on the number of participants screened who refused to participate. • **Were the subjects asked to participate in the study representative of the entire population from which they were recruited?** ○ Unclear; the authors did not report on

Table A6: Strengths and Limitations of Non-Randomized Studies using the Downs and Black Checklist[11]

Strengths	Limitations
○ Yes • **Does the study provide estimates of the random variability in the data for the main outcomes?** ○ Yes • **Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?** ○ Yes • **Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?** ○ Unclear; the number and types of centres involved were not reported. However, the setting was within the VA system so most likely representative. • **Were the statistical tests used to assess the main outcomes appropriate?** ○ Yes • **Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?** ○ Yes – there was some adjustment in the statistical models for some potential confounders. • **Were the main outcome measures used accurate (valid and reliable)?** ○ Yes	recruitment. • **Have the characteristics of patients lost to follow-up been described?** ○ No description of those who were lost to follow-up or noncompleters. This was a significant proportion for some outcomes (34%). • **Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance <5%** ○ Unclear • **Was compliance with the interventions reliable?** ○ 34% dropped out without completing therapy • **Were losses of patients to follow-up taken into account?** ○ 34% of patients did not complete therapy and were missing outcome data. This was not accounted for in the analysis.
Wasler et al., 2013[20]	
• **Is the hypothesis/aim/objective of the study clearly described?** ○ Yes • **Are the main outcomes to be measured clearly described in the Introduction or Methods section?** ○ Yes • **Are the characteristics of the patients included in the study clearly described?** ○ Some characteristics were described • **Are the interventions of interest clearly described?** ○ Yes • **Are the main findings of the study clearly described?** ○ Yes • **Does the study provide estimates of the random variability in the data for the main outcomes?** ○ Yes • **Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than**	• **Have all important adverse events that may be a consequence of the intervention been reported?** ○ No adverse event reporting • **Were those subjects who were prepared to participate representative of the entire population from which they were recruited?** ○ Unclear; the authors did not report on the number of participants screened who refused to participate. • **Were the subjects asked to participate in the study representative of the entire population from which they were recruited?** ○ Unclear; the authors did not report on recruitment. • **Have the characteristics of patients lost to follow-up been described?** ○ No description of those who were lost to follow-up or non-completers. This was a significant proportion for some outcomes (32%).

Table A6: Strengths and Limitations of Non-Randomized Studies using the Downs and Black Checklist[11]

Strengths	Limitations
0.001? ○ Yes • **Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?** ○ Yes. The paper describes the United States Veterans Health Administration's national approach to ACT delivery for veterans with depression. • **Were the statistical tests used to assess the main outcomes appropriate?** ○ Yes • **Were the main outcome measures used accurate (valid and reliable)?** ○ Yes	• **Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance <5%?** ○ Unclear • **Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?** ○ No • **Was compliance with the interventions reliable?** ○ 32% dropped out without completing therapy • **Were losses of patients to follow-up taken into account?** ○ 32% of patients did not complete therapy and were missing outcome data. This was not accounted for in the analysis.

ACT = Acceptance and commitment therapy; VA = Veteran's Affairs

Appendix 4: Main Study Findings and Author's Conclusions

Table A7: Summary of Findings of Included Systematic Reviews

Main Study Findings	Author's Conclusion
Bluett et al. 2014[15]	
• Three case studies of ACT used in adults with PTSD, one of which was a veteran. • One of the other case studies involved a patient with PTSD and substance abuse, while the other involved PTSD and depression. • All case studies demonstrated preliminary support for ACT.	No conclusions were made specific to PTSD, however, more generally, the authors noted that "while the preliminary evidence for ACT and anxiety disorders is promising, more stringent research and methodology should be pursued." p. 621 and "in order for ACT to be considered a well-established treatment for anxiety disorders studies should include control comparison groups, larger sample sizes, and blind assessment. In addition, few studies reported assessment of treatment adherence. Therefore it cannot be fully determined whether the treatments provided in the reviewed studies are consistent with the theory, philosophy, and model of ACT." (p621)
Swain et al. 2013[14]	
• One study compared ACT and ACT without the 'discovering the self' phase in 15 veterans. Both groups had a decrease in PTSD scores, less symptoms and less distress. The only statistically significant difference was for self-reported PTSD symptoms, which favoured ACT. • In a study with a nonequivalent control group design, 12 veterans who received ACT experienced an increase in automatic thoughts relative to demographically matched controls without PTSD. • In a case study in which a woman received 21 individual ACT sessions to manage chronic PTSD and major depressive disorder, she experienced an improvement in PTSD severity and anxiety. • All of the literature for PTSD included in this systematic review was rated below average for quality.	"Taken together it is difficult to draw firm conclusions about the effectiveness for ACT in the treatment of PTSD at this stage due to both the low number of studies available and the methodological caveats reflected in low POMFR scores. More research is required to gain further knowledge about the suitability of ACT for this population." (p973)

ACT = Acceptance and commitment therapy; POMFR = Psychotherapy outcome study methodology rating form; PTSD = Post-traumatic stress disorder

Table A8: Summary of Findings of Included Clinical Studies

<table>
<tr><th>Main Study Findings</th><th>Author's Conclusion</th></tr>
<tr><td colspan="2">Randomized Controlled Trials</td></tr>
<tr><td colspan="2">Boals et al., 2016[16]</td></tr>
<tr><td>
PCL-S[A] – Mean (SD)
<table>
<tr><th></th><th>Pretreatment</th><th>Post</th><th>6 Weeks Post</th></tr>
<tr><td>ACT + TAU</td><td>60.0 (10.4)</td><td>45.0 (13.8)</td><td>43.3 (14.5)</td></tr>
<tr><td>TAU Only</td><td>55.9 (10.7)</td><td>51.3 (13.8)</td><td>47.1 (13.2)</td></tr>
</table>
Time 1 to Time 2; P= <0.01
Time 1 to Time 3; P = NS

BDI-II – Mean (SD)
<table>
<tr><th></th><th>Pre-treatment</th><th>Post</th><th>6 Weeks Post</th></tr>
<tr><td>ACT + TAU</td><td>30.7 (12.4)</td><td>21.7 (10.7)</td><td>19.6 (13.0)</td></tr>
<tr><td>TAU Only</td><td>25.4 (13.2)</td><td>25.0 (13.0)</td><td>22.6 (15.1)</td></tr>
</table>
Time 1 to Time 2; P= <0.01
Time 1 to Time 3; P < 0.05
</td><td>"The addition of ACT to TAU led to significant decreases in event centrality, PTSD symptoms, and depression. Specifically, participants assigned to receive ACT sessions reported lower PTSD symptoms, less depression, and less event centrality at the posttreatment session." (p481)</td></tr>
<tr><td colspan="2">Lang et al. 2016[4]</td></tr>
<tr><td>
Primary Outcomes (Up to 12 Months of Follow-Up)

Brief Symptom Inventory-18 Global Severity Index[B] (ACT vs PCT)
• Mean Difference in Change from Baseline to Post-Treatment
  ○ -0.53 (95% CI, -4.35 to 3.28)
• Mean Difference in Change from Baseline to 3 months
  ○ 0.33 (95% CI, -3.72 to 4.37)
• Mean Difference in Change from Baseline to12 months
  ○ -0.69 (95% CI, -5.89 to 4.51)

Sheehan Disability Scale [B] (ACT vs PCT)
• Mean Difference in Change from Baseline to Post-Treatment
  ○ -0.58 (95% CI, -1.23 to 0.07)
• Mean Difference in Change from Baseline to 3 months
  ○ -0.69 (95% CI, -1.61 to 0.24)
• Mean Difference in Change from Baseline to 12 months
  ○ -0.88 (95% CI, -2.22 to 0.46)

Secondary Outcomes (Only Measured at Post-Treatment)

PHQ-9 (ACT vs PCT)
• Mean Difference in Change from Baseline to Post-Treatment[B]
  ○ 0.68 (95% CI, -1.37 to 2.73)
PCL-M (ACT vs PCT)
• Mean Difference in Change from Baseline to Post-Treatment[B]
  ○ -3.38 (95% CI, -7.76 to 0.99)
</td><td>"ACT performed similarly to an active control condition, and the effect sizes were modest. At present, our findings suggest ACT may not be a first-line approach among veterans with specific diagnoses, who may do better with established evidence-based therapies. Given that it led to reliable change within a subgroup, it is possible that it is a good match for some veterans and may be reasonable to implement with nonresponders to other approaches." (p. 10)</td></tr>
</table>

Table A8: Summary of Findings of Included Clinical Studies

Main Study Findings	Author's Conclusion

DAR-II (ACT vs PCT)
• Mean Difference in Change from Baseline to Post-Treatment[B]
  ○ -0.40 (95% CI, -2.37 to 1.57)
WHOQOL-BREF Physical (ACT vs PCT)
• Mean Difference in Change from Baseline to Post-Treatment[C]
  ○ 2.40 (95% CI, -2.86 to 7.64)
WHOQOL-BREF Psychological (ACT vs PCT)
• Mean Difference in Change from Baseline to Post-Treatment[C]
  ○ -0.48 (95% CI, -5.92 to 4.97)
WHOQOL-BREF Social (ACT vs PCT)
• Mean Difference in Change from Baseline to Post-Treatment[C]
  ○ 6.97 (95% CI, -0.56 to 14.51)
WHOQOL-BREF Environmental (ACT vs PCT)
• Mean Difference in Change from Baseline to Post-Treatment[C]
  ○ 1.37 (95% CI, -3.60 to 6.34)
SF-12 Physical Composite Score (ACT vs PCT)
• Mean Difference in Change from Baseline to Post-Treatment[C]
  ○ -1.60 (95% CI, -4.35 to 1.15)
SF-12 Mental Health Composite Score (ACT vs PCT)
• Mean Difference in Change from Baseline to Post-Treatment[C]
  ○ 2.46 (95% CI, -1.87 to 6.80)	

Non-randomized Studies	
Fiorillo et al., 2017[17]	
PCL-5 – Mean (SD) Pre-treatment: 38.86 (15.05) Post-treatment: 21.19 (16.68) *P* < 0.001 **DASS21** Depression Scale – Mean (SD) Pre-treatment: 20.09 (12.80) Post-treatment: 13.52 (12.01) *P* < 0.01 Anxiety Scale – Mean (SD) Pre-treatment: 13.33 (9.13) Post-treatment: 7.52 (6.90) *P* < 0.001	**"***The study provides important new evidence that a web-based ACT program for survivors of interpersonal trauma may be acceptable, safe, and helpful. A next step would be to examine an updated version of this program using a randomized controlled trial that includes follow-up data.***"** (p111)
Glover et al., 2016[18]	
DASS21 Depression Scale – Mean (SD) Pre-treatment: 19.97 (10.34)	*"The current study provides preliminary evidence for the efficacy of a FACT group protocol in a VA primary care setting. Moreover, the brief, group-based, and*

Table A8: Summary of Findings of Included Clinical Studies

Main Study Findings	Author's Conclusion
Post-treatment: 15.27 (9.51) *P* < 0.001 Anxiety Scale – Mean (SD) Pre-treatment: 13.30 (8.70) Post-treatment: 11.40 (9.48) *P* =0.07 Stress Scale – Mean (SD) Pre-treatment: 19.73 (9.69) Post-treatment: 17.19 (9.68) *P* = 0.04 **SF-12** Physical Composite Score – Mean (SD) Pre-treatment: 35.48 (8.73) Post-treatment: 38.06 (8.80) *P* = 0.01 Mental Health Composite Score – Mean (SD) Pre-treatment: 35.87 (9.17) Post-treatment: 40.41 (8.64) *P* = 0.003 **WBI-5** – Mean (SD) Pre-treatment: 8.60 (4.16) Post-treatment: 12.81 (5.34) *P* < 0.001	*transdiagnostic nature of the intervention employed in this study represents an ideal fit for the needs of modern primary care. For these reasons, FACT represents a promising intervention that can advance the goals of integrated primary care."* (p160)
Wasler et al., 2015[19]	
BDI-II – Mean (SD) Pre-treatment: 30.8 (10.7) Post-treatment: 15.3 (9.5) *P* < 0.001[D] **Suicidal Ideation (% Yes)** Pre-treatment: 55.8% Post-treatment: 34.7% *P* < 0.001[E]	*"In summary, veterans receiving ACT-D, on average, achieved significant reductions in depression severity and suicidal ideation during the course of treatment."* (p30) *"These findings, taken together, provide support for the utility and effectiveness of ACT-D in the treatment of depression and suicidal ideation."* (p30)
Wasler et al., 2013[20]	
BDI-II – Mean (SD) Pre-treatment: 30.5 (NR) Post-treatment: 19.4 (5.6) *P* < 0.001 **WHOQOL domains** (Psychological, Physical, Social, Environmental) were all reported to have increased significantly (*P* < 0.001) but numerical data were not presented.	*"Overall, the data yielded by this program evaluation indicate that training in and implementation of ACT-D in routine clinical settings resulted in significant increases in therapist competency and improvements in depression and quality of life among Veterans. Accordingly, ACT-D appears to be a valuable treatment option for training and dissemination in a variety of clinical settings. Additional evaluation and controlled research on ACT-D with Veterans are encouraged to supplement the current findings."* (p562)

ACT = Acceptance and commitment therapy; ACT-D = Acceptance and commitment therapy for depression; BDI-II = Beck Depression Inventory-II; DASS-21 = Depression Anxiety and Stress Scale 21; DAR-II = Dimensions of anger reactions; DSM= Diagnostic and Statistical Manual of Mental

Disorders; FACT = Focused acceptance and commitment therapy; HRQoL = Health-related quality of life; NR = Not reported; PHQ-9: Patient Health Questionnaire 9; PCL-S = PTSD Checklist Specific; PTSD = Post-traumatic stress disorder; RCT = randomized controlled trial; SD = Standard deviation; SF-12 = Short Form 12; SI = Suicidal Ideation; TAU = Treatment as usual; VA = Veteran's Affairs; WBI-5 = WHO-5 Well Being Index; WHOQOL-BREF = World Health Organization Quality of Life Scale, Brief

[A] The PCL-S is a measure of PTSD symptoms. Lower score indicate fewer symptoms.
[B] A negative difference favours ACT
[C] A positive difference favours ACT
[D] Result is from a mixed model that included other covariates (age, gender, race, time, baseline suicidal ideation, and time by suicidal ideation interaction)
[E] Result is from a mixed model that included other covariates (age, gender, race, time, experiential acceptance, and mindfulness)